

# Infarct-related artery patency before primary percutaneous coronary intervention for myocardial infarction: a blessing in disguise?

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This year, we are celebrating the 40th anniversary of the first successful percutaneous coronary intervention (PCI) performed by Andreas Grüntzig in September 1977. Five years later, the first successful PCI in acute ST-segment elevation myocardial infarction (STEMI) was conducted by Jürgen Meyer. Since then, a rapid development in the procedural technique and concomitant pharmacotherapy has been observed, leading to a reduction in mortality of patients presenting with STEMI. Despite this progress, the time from symptom onset to successful reperfusion and the preprocedural patency of the infarct-related artery (IRA) still remain important determinants of outcomes in patients with STEMI.<sup>1-4</sup>

The presence of the patent IRA, frequently defined as the Thrombolysis in Myocardial Infarction (TIMI) flow grade 2/3, before primary PCI for STEMI, was shown to be associated with improved short- and long-term mortality rates.<sup>1,3,4</sup> The mechanism underlying the observed survival benefit might be related to less pronounced ischemia in the setting of preserved blood flow and oxygen supply. Also, achievement of spontaneous or pharmacologically induced early reperfusion may reduce the duration of ischemia (by early restoration of flow) and thus prevent irreversible myocardial injury.<sup>2</sup> In addition, the presence of the patent IRA may indicate lower thrombus load and better visualization of the vessel.<sup>1</sup> Thus, it may facilitate the procedure by allowing a better selection of stent size or length and reducing the risk of complications, including distal embolization. As a result, initial IRA patency is frequently associated with complete reperfusion after primary PCI not only on the epicardial level (postprocedural TIMI grade 3 flow) but also on the microcirculation level (myocardial blush grade 3, complete ST-segment resolution).<sup>5</sup> Importantly, the achievement of full reperfusion on both levels is the main goal of primary PCI.

However, according to the study by Karwowski et al,<sup>6</sup> published in the current issue of the *Polish Archives of Internal Medicine*, the mortality benefit of the patent IRA before primary PCI for STEMI may be limited only to patients with STEMI related to stenosis or occlusion of the left anterior descending artery (LAD). This observation is quite obvious as the possible benefits of IRA patency are especially pronounced in high-risk patients with a large area of the myocardium at risk. These high-risk population includes predominantly patients with LAD-related STEMI, because the LAD supplies a large proportion of the left ventricular myocardium.

In line with the above findings, previous studies confirmed that mortality benefits from pharmacologically induced early reperfusion in patients with STEMI using intravenous abciximab are limited only to high-risk individuals, including those with anterior-wall STEMI.<sup>7</sup> On the other hand, the lack of clear mortality benefits from the patent IRA in patients with STEMI related to the left circumflex artery (LCx) and the right coronary artery (RCA) cannot be explained by the differences in the risk among the groups as the long-term mortality and prevalence of Killip class of 3 or higher on admission were quite comparable.<sup>6</sup>

As suggested by Karwowski et al,<sup>6</sup> the lack of the expected benefit is probably associated with a lower area of the myocardium at risk in patients with STEMI related to the LCx or RCA compared with those with LAD-related STEMI. However, despite the enrollment of over 4500 patients with STEMI, the results of subgroup analyses should be interpreted with caution, and strong statements concerning the lack of benefit should be avoided. Also, quite surprisingly, patients with TIMI grade 1 flow were included in the group with total occlusion. In contrast, most of the previous studies compared patients with TIMI grade 0/1 flow (occluded artery) versus 2/3 flow (patent artery).<sup>1-4</sup>

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Received: June 12, 2017.

Accepted: June 12, 2017.

Published online: June 30, 2017.

Conflict of interest: none declared.

Pol Arch Intern Med. 2017;

127 (6): 383-385

doi:10.20452/pamw.4055

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By definition, TIMI grade 1 flow is faint antegrade coronary flow beyond the occlusion, with incomplete filling of the distal coronary bed (contrast media penetration without perfusion). Therefore, the risk of potential events in the patent-IRA group was increased, limiting the possible difference between the groups.

Another possible limitation is the lack of an independent core laboratory assessment of flow within the IRA. On the other hand, the largest variability in the assessment of TIMI flow is noted for differentiation between TIMI grade 2 and TIMI grade 3. Thus, in this particular case, due to the aggregate analysis of TIMI flow grades 1–3, the results might not have been affected by the analysis based only on the judgment of the primary PCI operator. Also, the overall risk of the study population was decreased by exclusion of patients with previous MI. The patency of the IRA seems to be particularly important in those patients. In the presence of necrotic regions following MI or of non-IRA-related chronic total occlusions, early reperfusion may reduce the risk of hemodynamic instability and cardiogenic shock.<sup>8</sup> Interestingly, the chance of early reperfusion might be affected by delay to PCI. In the discussed study, time from symptom onset to PCI was longer in patients with the patent IRA before PCI.<sup>6</sup> Other studies also reported longer delay from baseline electrocardiogram (the moment of early pharmacotherapy administration) to PCI in patients with the patent IRA than those without.<sup>1,9</sup> Thus, it may suggest a higher value of pharmacologically induced early reperfusion in primary-PCI networks with expected longer transfer-related delays. Unfortunately, the authors did not report data on pharmacotherapy and possible impact of early pharmacotherapy on the IRA patency. On the other hand, the enrollment period was limited to 2008; thus, the applicability of such data in the light of modern adjunctive pharmacotherapy and improved logistics would be rather limited.<sup>10–12</sup> Fortunately, a recent report from the EUROMAX trial<sup>1</sup> has confirmed that despite progress in primary PCI strategies, early IRA patency is still associated with higher procedural success and improved clinical outcomes.

In contrast to STEMI, the impact of the pre-procedural patency of the IRA in patients with NSTEMI is less well established. It is partially related to a large heterogeneity of angiographic pictures, from a totally occluded coronary artery, through a severely stenosed artery with a ruptured plaque, to nonobstructive coronary artery disease observed in patients with NSTEMI. Karwowski et al<sup>6</sup> dealt with possible heterogeneity by including patients undergoing PCI and thus limiting the risk of other diagnoses. Also, in patients with NSTEMI, the area of the myocardium at risk might be lower than in patients with STEMI. Thus, confirmation of the impact of the patent IRA on mortality in patients with NSTEMI can be difficult. Both in the ACUITY study and in the Polish Registry of Acute Coronary Syndromes, long-term

mortality rates were comparable between patients with and without the occluded IRA before PCI.<sup>6,13</sup> However, Karwowski et al<sup>14</sup> stressed the possible impact of LCx occlusion on in-hospital mortality. It might be related to some difficulty in detection of LCx-related ischemia by standard 12-lead electrocardiogram (ECG) and possible prolongation of time to reperfusion. On the other hand, in patients with inconclusive electrocardiogram results and signs of ongoing myocardial ischemia, current guidelines strongly recommend the recording of additional leads ( $V_7$ – $V_9$  and  $V_3R$ – $V_4R$ ).<sup>14</sup> Also, rapid “rule-in” and “rule-out” of MI is possible using high-sensitive cardiac troponin assays.<sup>14</sup> Importantly, it may result in reduced delay to coronary angiography and PCI in patients with NSTEMI. Thus, the results of the study conducted in 2008 may not be applicable to current clinical practice.

Similarly to the STEMI group, no data on adjunctive pharmacotherapy were provided. Results of the ACUITY study have suggested that administration of unfractionated heparin, P2Y<sub>12</sub> inhibitors, or abciximab was associated with lower rates of the occluded IRA at baseline.<sup>13</sup> However, routine pretreatment with P2Y<sub>12</sub> inhibitors in patients with NSTEMI, especially those with low-to-intermediate risk, is not recommended. It is related to the lack of clear clinical benefit and elevated risk of bleeding in case of urgent coronary artery bypass grafting related to pretreatment.<sup>11,14</sup>

Despite a limited mortality benefit in some subgroups of patients, early IRA patency will be still welcomed by numerous interventional cardiologists before conducting PCIs for acute MI. It may be potentially promoted by early pharmacotherapy. However, early pharmacotherapy strategies should be adjusted for clinical presentation (STEMI, NSTEMI), logistics, and both ischemic and bleeding risk profiles.<sup>11</sup> Optimization of pharmacotherapy should be accompanied by continuous efforts to reduce time from symptom onset to successful reperfusion. Importantly, as suggested by Karwowski et al,<sup>6</sup> even the presence of the patent IRA does not mean the best long-term prognosis.<sup>15</sup> Thus, improvement of each stage of MI treatment (pre-, in-, and post-hospital stages) still seems to be justified to improve outcomes.<sup>11</sup>

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